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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,273	08/07/2002	Michel Perricaudet	ST99019 US PCT	8299

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EXAMINER	
BOESEN, AGNIESZKA	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,273	PERRICAUDET ET AL.	
	Examiner	Art Unit	
	Agnieszka Boesen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-11,13-15 and 17-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-11,13-15 and 17-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication received September 22, 2006.

Election/Restrictions

Applicant's election without traverse of species of human iodine transporter NIS, promoter derived from regulatory sequence of the elastase I; adenovirus of human type Ad2 or Ad5; CMV viral promoter; and deletion of all or part of E1 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Thus the restriction is deemed proper and is made FINAL.

Claims 1-5, 7-11, 13-15, and 17-32 are pending and under examination.

Priority

Acknowledgment is made for foreign priority to PCT/FR00/01594.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7-11, 13-15, and 17-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims are indefinite for reciting "iodine transporter, (Na+/I) NIS or derivative thereof" because the exact meaning of the phrase is not clear.

The term "derivative" is not one which has a universally accepted meaning in the art nor is it one which has been adequately defined in the specification. The primary deficiency in the use of this phrase is the absence of an ascertainable meaning for said phrase. Since it is unclear how the iodine transporter is to be derived to yield the class of derivatives referred to in the claims, there is no way for a person of skill in the art to ascribe a discrete and identifiable class of compounds to said phrase. Further, it is not clear whether the derivative is formed by attachment of another gene, detectable marker, therapeutic molecule, or some other molecule. In addition, since the term "derivative" does not appear to be clearly defined in the specification, and the term can encompass any nucleic acids encoding for various functional genes. In absence of a single defined art recognized meaning for the phrase and lacking a definition of the term in the specification, one of skill in the art could not determine the metes and bounds of the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-5, 7-11, 13-15, and 17-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims are drawn to a defective recombinant adenovirus encoding the specific iodine transporter or a derivative thereof. The specification does not provide a sufficient written description for the derivative of iodine transporter (Na+/I) NIS as it

does not define what are the structures of the claimed derivatives and how would the derivative structures change or preserve the desired function of the iodine transporter gene.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. One would be unable to envision the structures of derivatives encompassed by the current claims. Applicant has not provided a core region of the derivatives that must be conserved in order to retain the claimed function. Lacking this information there is no structure/function correlation upon which one can design the encompassed derivative iodine transporter genes encoded within the recombinant adenovirus. One would be unable to predict if the claimed iodine transporter derivatives would be capable to maintain the expected function such as expression under the control of a promoter in tumor cells. The only factor present in the claim is the specific iodine transporter gene under control of transcriptional promoter. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at

page 1116). As discussed above, the skilled artisan cannot envision the structures of the iodine transporter derivatives encompassed by the claims, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of designing a recombinant adenovirus encoding iodine transporter derivatives. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-5, 7-9, 11, 13, 19, 22, 24, 26, 28, 30, and 31 are rejected under 35 U.S.C. 102(a) as being anticipated by Cho et al. (Gene Therapy, May 2000, Vol. 7, p. 740-749, Abstract in IDS of 6/30/2003).

Because the English copy of the foreign priority document has not been provided, the current claims are given priority to PCT/FR00/01594. English copy of the priority document would help overcome this rejection.

Claims are drawn to a defective adenovirus comprising at least one DNA sequence encoding the specific human iodine transporter (Na+/I) NIS, wherein DNA sequence is placed

under the control of CMV promoter. The adenovirus is a human adenovirus type Ad2 or Ad5. The recombinant adenovirus comprises deletions of all or part of an E1 region.

Cho et al. disclose expression of human iodine transporter (Na+/I) NIS in replication-deficient/defective recombinant adenovirus Ad5 under control of CMV promoter (see the entire document, particularly Materials and Methods and Results). The recombinant adenovirus disclosed by Cho et al., comprises deletions in E1 region (see Materials and Methods and Figure 1). Thus by this disclosure Cho et al. anticipate the current claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7-9, 11, 13, 15, 17-19, 21, 22, 24, 26, 28, 30, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mandell et al. (Cancer Research, February 1999, Vol. 59, p. 661-668, IDS of 12/7/2001) in view of Wilson et al. (US Patent 5,652,224).

Claims are drawn to a defective adenovirus comprising at least one DNA sequence encoding the specific human iodine transporter (Na+/I) NIS, wherein DNA sequence is placed under the control of CMV promoter. The adenovirus is a human adenovirus type Ad2 or Ad5. The recombinant adenovirus comprises deletions of all or part of an E1 region. Claims are also drawn to pharmaceutical composition comprising the defective recombinant adenovirus

encoding the specific human iodine transporter (Na+/I) NIS in a physiologically acceptable vehicle. The pharmaceutical composition comprises between 10^4 and 10^{14} pfu/ml.

Mandell et al. teach retroviral vector comprising DNA sequence encoding rat iodine transporter (Na+/I) NIS gene. Mandell et al. teach that the retroviral vector encoding rat iodine transporter (Na+/I) NIS allows expression of iodine transporter gene in tumor cells (see Materials and Methods and Results on page 663). Mandell et al., does not teach human iodine transporter or an adenovirus vector, however Mandell et al., teaches that NIS-based therapy may have both therapeutic and diagnostic applications for cancer and that his approach should be adaptable to other gene delivery methods allowing development of human clinical trials using NIS gene as an anti-tumor agent (see abstract and Discussion on page 667).

Wilson et al. teach Ad2 and Ad5 adenoviral vector and its application for gene delivery to all cell types (see column 2, lines 53-59, and column 9, lines 4-6). Wilson et al. teach deletion in E1 region that makes the adenovirus replication defective (column 10, lines 34-55, and claim 3). Wilson et al also teach CMV promoter (see column 19, line 4, column 32, line 19-22, Example 2, and Figure 6). Wilson et al. teach pharmaceutical composition in a physiologically acceptable vehicle (see claim 10). Wilson et al. teach pharmaceutical composition comprising between 10^9 and 10^{11} pfu/ml (see column 16, lines 10-21).

It would have been obvious to one of ordinary skill in the art to use adenoviral vector to express human iodine transporter (Na+/I) NIS gene.

One would have been motivated to express Mandell's human iodine transporter (Na+/I) NIS gene in Wilson's adenoviral vector, because Mandell teaches NIS-based therapy may have both therapeutic and diagnostic applications for cancer and that his approach should be adaptable

to other gene delivery methods allowing development of human clinical trials using NIS gene as an anti-tumor agent, and because Wilson teaches that adenoviral vectors are suitable for expression of transgenes in different cell types.

One would have had a reasonable expectation of success to make a construct of adenoviral vector and human iodine transporter (Na+/I) NIS because the recombinant technology has been known at the time the current invention was made as evidenced by Wilson.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mandell et al. (Cancer Research, February 1999, Vol. 59, p. 661-668, IDS of 12/7/2001) in view of Wilson et al. (US Patent 5,652,224) as applied to claims 1-5, and 7-9 and further in view of Sauvage (US Patent 6,022,708).

Claim is drawn to the defective adenovirus wherein the promoter is a regulatory sequence of the elastase I gene.

Mandel and Wilson teach the claim limitations as discussed above. Neither Mandell nor Wilson teach the limitation of regulatory sequence of the elastase I gene promoter. Sauvage et al. teach adenoviral vectors and inserting an elastase gene as an enhancer sequence into the viral vector. Sauvage et al. teach that elastase regulatory sequence acts on promoter to increase its transcription (see column 19, lines 23-48).

It would have been obvious to one of ordinary skill in the art to insert the regulatory sequence of the elastase I gene promoter in the defective recombinant adenovirus.

One would have been motivated to insert Sauvage's regulatory sequence of the elastase I gene promoter in Wilson's recombinant adenovirus, because Sauvage et al. teach that elastase regulatory sequence acts on promoter to increase its transcription.

One would have had a reasonable expectation of success to insert regulatory sequence of the elastase I gene promoter in recombinant adenovirus because the recombinant technology has been known at the time the current invention was made as evidenced by Wilson.

Claims 14, 20, 23, 25, 27, 29 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mandell et al. (Cancer Research, February 1999, Vol. 59, p. 661-668, IDS of 12/7/2001) in view of Wilson et al. (US Patent 5,652,224) as applied to claims 1-5, 7-9, 11, 13, 15, 17-19, 21, 22, 24, 26, 28, 30, and 31 and further in view of Hidaka et al. (Thyroid, 1996, Vol. 6, p. 23-28).

Claima are drawn to the defective adenovirus comprising a gene involved in peroxidase system comprising the gene for thyroperoxidase.

Mandel and Wilson teach the claim limitations as discussed above. Neither Mandel nor Wilson teach gene involved in peroxidase system comprising the gene for thyroperoxidase.

Hidaka et al. teach adenovirus Ad5 expressing thyroid peroxidase gene (see the entire document). Hidaka et al. also teach that thyroid peroxidase gene expression induced with adenovirus should facilitate understanding of T cell immunity to thyroid peroxidase in patients with autoimmune thyroid diseases (see abstract).

It would have been obvious to one of ordinary skill in the art to express thyroid peroxidase gene in addition of expressing iodine transporter in the adenoviral vector.

One would have been motivated to express Hidaka's peroxidase gene in addition of expressing iodine transporter in the adenoviral vector because Hidaka et al. teach that thyroid peroxidase gene expression induced with adenovirus should facilitate understanding of T cell immunity to thyroid peroxidase in patients with autoimmune thyroid diseases and because both iodine and thyroid peroxidase are involved in normal thyroid function.

One would have had a reasonable expectation of success to express a gene involved in peroxidase system comprising the gene for thyroperoxidase in recombinant adenovirus because the recombinant technology has been known at the time the current invention was made as evidenced by Wilson.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen whose telephone number is 571-272-8035. The examiner can normally be reached on 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AB

Agnieszka Boesen, Ph.D.

11/16/06

Stacy B. Chen 11/16/06

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PRIMARY EXAMINER